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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,790	01/29/2004	Mitsuo Nakamura	MO1720USCNT4	7499

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EXAMINER

CHANG, CELIA C

ART UNIT PAPER NUMBER

1625

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/767,790	Applicant(s) NAKAMURA ET AL.	
	Examiner Celia Chang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 29 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

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### DETAILED ACTION

1. This application is a continuation of SN 10/192,444 which is a continuation of SN 09/713,184 which is a continuation of SN 09//348,946 which is a continuation of SN 08/737,131. Claims 1-36 are as originally filed are pending.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 29-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. Pharm. World or Zamani et al. Chirality in view of Jacque et al. and Brenman et al. US 4,931,557 (all cited on 1449 of previous office action).

Determination of the scope and content of the prior art (MPEP §2141.01)

Enantiomerically pure terfenadines of applicant's claims have been conventionally prepared. (See Zhang and Zamani). Zhang et al. disclosed purified terfenadines with tartaric acid in more than 96% (see p.186) and diastereomer separation was achieved with both R is lower alkyl or carboxyl (see p.188). Zhang p.186, left column last paragraph wherein Zhang specifically disclosed Aterfenadine was resolved by the formation of diastereomeric salts with tartaric acid derivatives with the obtained physical data in specific rotation. Zamani et al. disclosed metabolically and HPLC pure terfenadines. Specifically, the Zamani reference disclosed a chiral salt formed with the chiral stationary phase which is evidenced by the elution of the free separated enantiomers (see p.468-469).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the claims and the prior art compounds is that instead of purifying through a stationary chiral salt (Zamani) or enantiomeric tartrate (Zhang) the instant claims are di-p-toluoyl tartarate and mandelate diastereoisomeric salts.

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

It is conventionally taught in the art that diatroyl tartarate and mandelate are optional choices for preparing resolvable diastereoisomeric salts (see Jacques et al. P.259 and 260). Further, the di-p-toluoyl tartarate was taught specifically to be equivalence for tartrate or mandelate (see Brennan >557 col. 3 table 1 and 2). The use of a polymeric chromatographic acid i.e. Zamani's polymeric chiral acid instead of a free acid i.e. applicants' chiral acid chosen among the many chiral acids of Jacques and Brennan, is considered prima facie obvious, see In re Apel 144 USPQ 748.

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In absence of unexpected results, there is nothing unobvious in choosing some among many of the enantiomeric acids to make new forms of old compounds. In re Cofer 148 USPQ 268.

3. Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. Pharm. World in view of Jacque et al. (Cited on 1449) and Brenman et al. US 4,931,557 (all cited on 1449 or previous office actions).

Determination of the scope and content of the prior art (MPEP §2141.01)

Enantiomerically pure terfenadines of applicant=s claims have been conventionally prepared by Zhang . Zhang et al. disclosed purified terfenadines with tartaric acid in more than 96% (see p.186) and diastereomer separation was achieved with both R is lower alkyl or carboxyl (see p.188). Zhang p.186, left column last paragraph wherein Zhang specifically disclosed Aterfenadine was **resolved** by the formation of diastereomeric salts with tartaric acid derivatives≡ with the obtained physical data in specific rotation.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the claims and the prior art compounds is that instead of purifying through an enantiomeric tartrate (Zhang ) the instant claims are di-p-toluoyl tartarate and mandelate diastereoisomeric salts.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

The resolution of chiral compounds into diastereoisomers using pure diastereoisomeric acid through formation of separable salts and recrystallization is conventional process in the chemical art. The instant claims using conventionally recognized optional choices of di-p-toluoyl tartarate or mandelate is also considered prima facie since di-p-toluoyl tartrate and mandelate are optional substitute for tartrate of Zhang et al.

Further, one having ordinary skill in the art would be motivated to substitute the tartrate of Zhang with di-p-toluoyl tartrate knowing that such di-p-toluoyl tartrate salt may form crystals which can be further purified through recrystallization (see Brennan col. 4 lines 35-40 and 50-55, heating, cooling, solid isolation).

In absence of unexpected results, there is nothing unobvious in carrying out an conventional process choosing an alternative conventional reagent among many. In re Lemin 141 USPQ 814.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. Pharm World Sci, or Terhechte et al. J. Chromat. A in view of Jacques et al. and Moutzka et al. US 3,452,086 (all cited previously).

Determination of the scope and content of the prior art (MPEP §2141.01)

Zhang et al. disclosed process and enantiomeric terfenadine of tartaric acid derivatives (see p.186), Terhechte et al. disclosed process of enantiomeric resolution in organic solvent and enantiomers of terfenadine chlorotartranilic acid (see p.220 section 2.3).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Zhang et al. or Terhechte disclosed all the elements of the claims **except** Zhang or Terhechte employed a different resolving chiral acid. Jacques et al. disclosed the variety of resolving acid (see 259-260) while Moutzka >086 disclosed the equivalent chloro-tartranilic acid and nitrotartranilic acid which is alternative choice for the other chiral resolving agents (see Jacques).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

Therefore, artisan in the field is in possession of process and purified terfenadine tartrate (Zhang) and terfenadine chlorotartranilic acid (Terhechte), with conventional choices of di-toluoyltartrate and mandelate (Jacques) and equivalency between chlorotartranilic acid and nitrotartranilic acid which are equivalent to the other tartrate derivative (Jacques). In absence of unexpected result, there is nothing unobvious in choosing some among many. In re Lemin 141 USPQ 814.

5. This is a third continuation of applicant's earlier Application No. 10/192,444, 09/348,946, 09/713,184 or 08/737,131. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


6. The references recited on 1449 was filed in the parent cases which were not in electronic version. It is recommended that copies of 1449 and references be made in the instant electronic file by submitting together with applicants' response.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to 790 whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

*OACS/Chang*  
*Mar. 9, 2005*

  
*Celia Chang*  
*Primary Examiner*  
*Art Unit 1625*